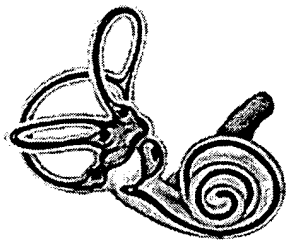

Vestibular System Primer

by David Dickman, Ph.D.

Humans have the ability to control posture and movements of the body and eyes relative to the external e vestibular system mediates these motor activities through a network of receptors and neural elements. Th integrates peripheral sensory information from vestibular, somatosensory, visceromotor, and visual recep motor information from the cerebellum and cerebral cortex. Central processing of these inputs occurs rap output of the vestibular system providing an appro priate signal to coordinate relevant movement reflexe vestibular system is considered to be a special sense, most vestibular activity is conducted at a subconsci However, in situations producing unusual or novel vestibular stimulation, such as rough air in a plane fli motion on ships, vestibular perception becomes acute, with dizziness, vertigo, or nausea often resulting.

Overview

The vestibular system is an essential component in the production of motor responses that are crucial for and survival. Throughout evolution, the highly conserved nature of the vestibular system is re vealed thr similarities in the anatomic or ganization of receptors and neuronal connections in fish, reptiles, birds, ar

For the present discussion, the vestibular system can be divided into five components: (1) The peripheral apparatus resides in the inner ear and is respon sible for transducing head motion and position into neura The central vestibular nuclei comprise a set of neurons in the brainstem that are responsible for receiving distributing information that controls motor activities such as eye and head movements, postural reflexes dependent autonomic reflexes and spatial orientation. (3) The vestibulo-ocular network arises from the v and is involved in the control of eye move ments. (4) The vestibulospinal network coordinates head mov musculature, and postural reflexes. (5) The vestibulo-thalamo-cortical network is responsible for the con of movement and spatial orientation.

Peripheral Vestibular Labyrinth

The vestibular labyrinth contains specialized sensory receptors and is located lateral and posterior to the inner ear (Fig. 1). The vestibular labyrinth consists of five separate receptor structures, three semicircula otolith organs, which are contained in the petrous portion of the temporal bone. The labyrinth is actually distinct components. The bony labyrinth is a surrounding shell that contains and protects the sensitive un tibular sensory structures (see Fig. 1). In humans, the bony labyrinth can be visualized only on excision c process. Inside the bony labyrinth is a closed, fluid-filled system, the membranous labyrinth, which cons tubes and prominences (Fig. 2). Vestibular receptors are located in special ized regions of the membrano

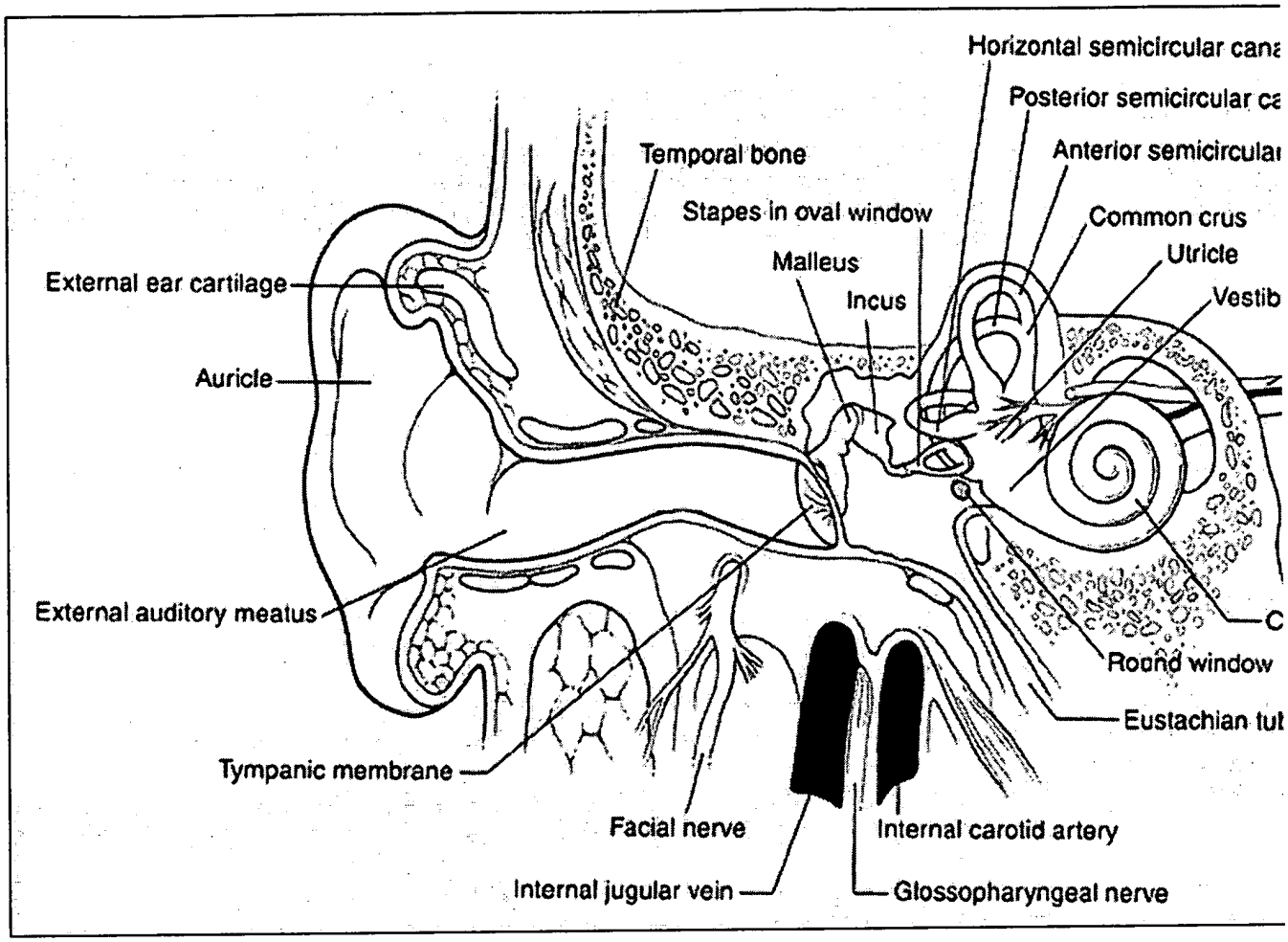

Figure 1. Cross section of the outer, middle, and inner ear.

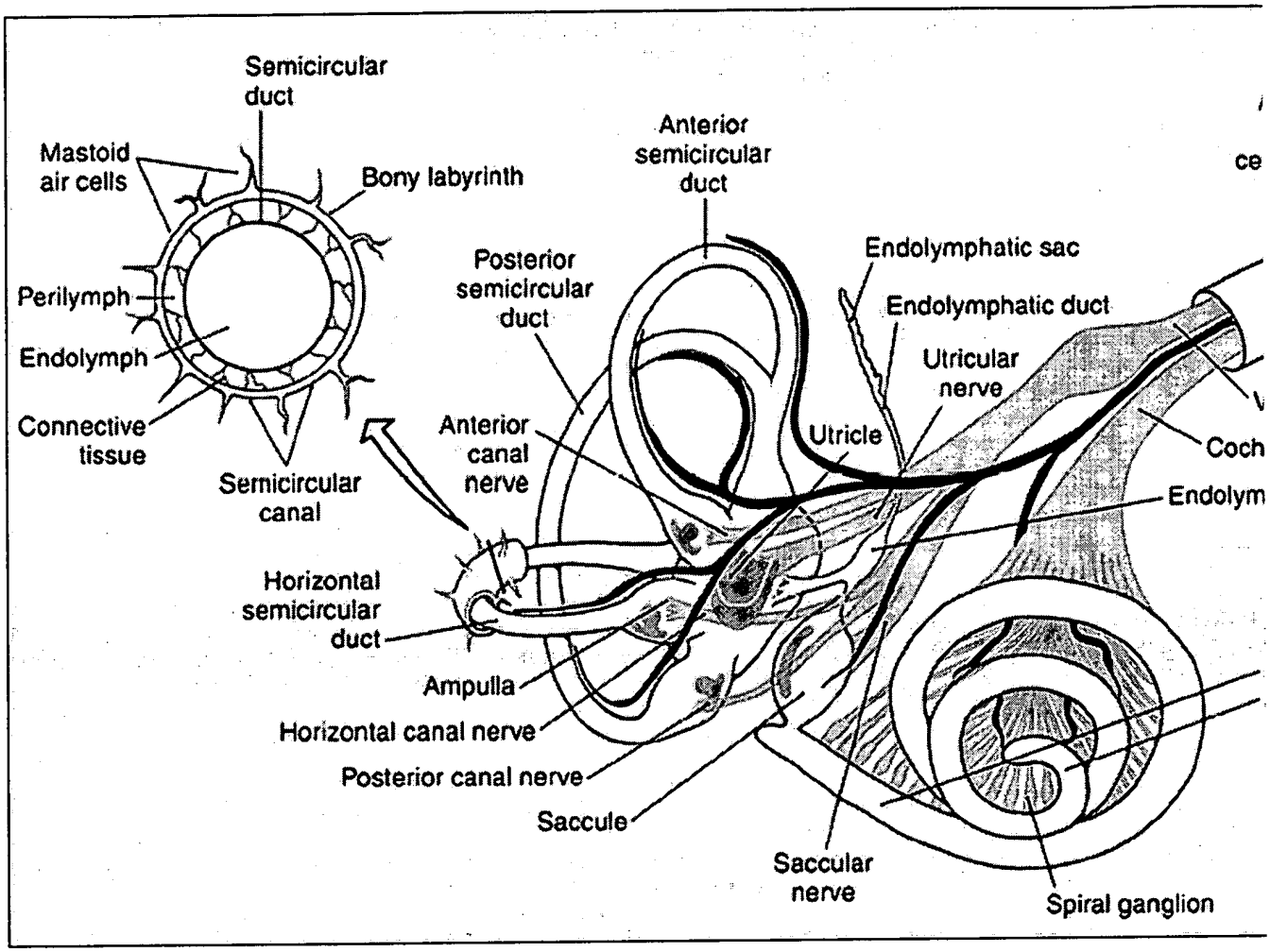

Figure 2. The membranous labyrinth and associated vessels and nerves.

Between the membranous and bony labyrinth is a space containing fluid called perilymph, which is simi cerebrospinal fluid. Perilymph has a high sodium content (150 mM) and a low potassium content (7 mM the vestibular portion of the eighth cranial nerve.

The membranous labyrinth is filled with a different type of fluid, called endolymph, which covers the sp receptors of both the vestibular and the auditory systems. Endolymph has a high concentra tion of potass and a low concentration of sodium (16 mM). It is important to note the differ ences in these two fluids b involved in the normal functioning of the vestibular system. Dis turbances in the distribution or ionic co lymph often lead to vestibular pathology.

Vestibular Receptor Organs. The five vestibular re ceptor organs in the inner ear complement each The semicircular canals (horizontal, ante rior, and posterior) transduce rotational head move ments (ang The otolith organs (utricle and saccule) respond to translational head movements (linear accelerations) o of the head relative to gravity. Each semicircular canal and otolith organ is spatially aligned to be most s movements in specific planes in three-dimen sional space.

In humans, the horizontal semicircular canal and the utricle both lie in a plane that is slightly tilted ante to the naso-occipital plane (Fig. 3). When a person walks or runs, the head is normally declined (pitched approximately 30 degrees, so that the line of sight is directed a few meters in front of the feet. This orien plane of the horizontal canal and utricle to be parallel with the earth horizontal and perpendicular to grav

and posterior semicircular canals and the sac cule are arranged vertically in the head, orthogonal to the h semicircular canal and utricle (see Fig. 3). The two vertical canals in each ear are positioned orthogonal t whereas the plane of the anterior canal on one side of the head is coplanar with the plane of the contralat canal (see Fig. 3).

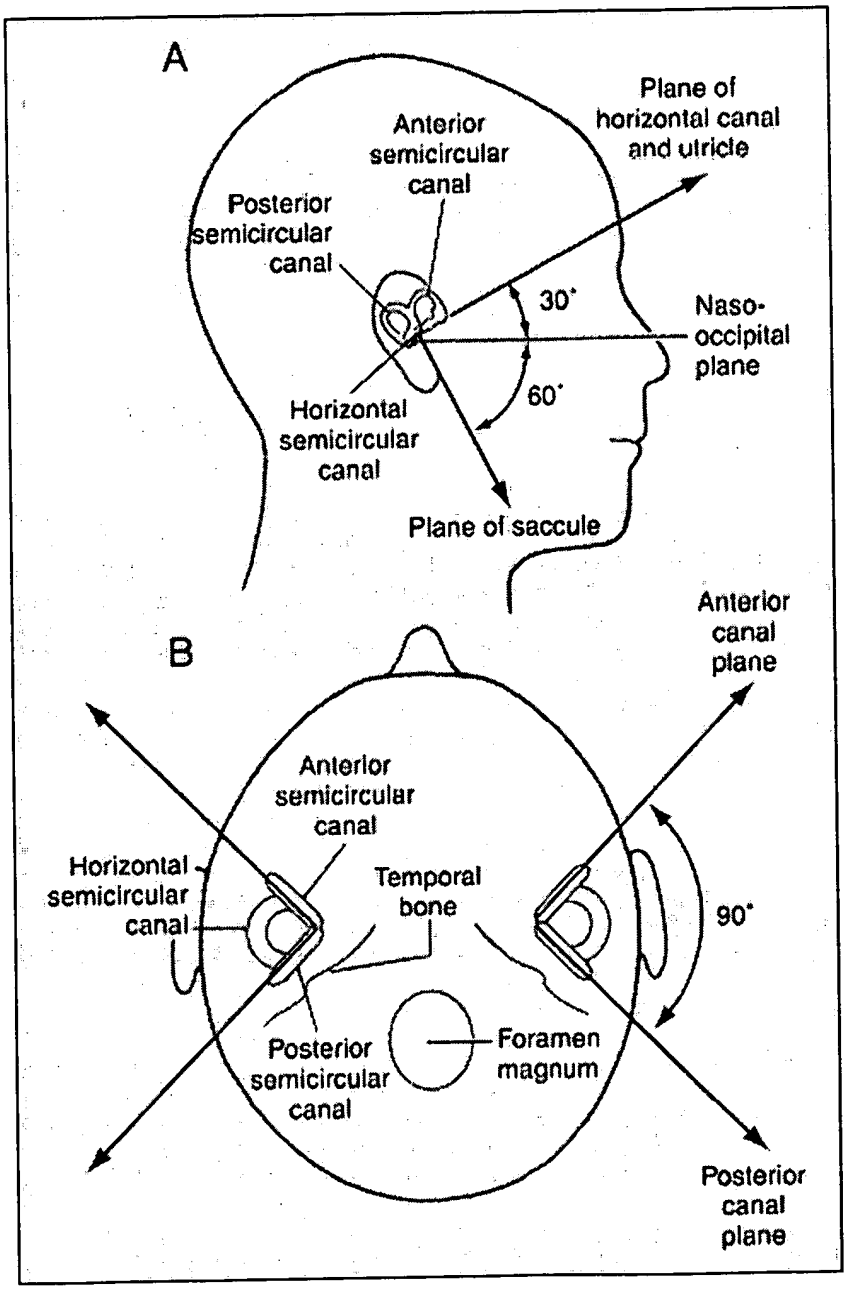

Figure 3. Orientation of the vestibular receptors. In the lateral view (A), the horizontal semicircular cana lie in a plane that is tilted relative to the naso-occipi tal plane. In the axial view (B), the vertical semicirc right angles to each other.

The receptor cells in each vestibular organ are in nervated by primary afferent fibers that join with those to comprise the vestibulocochlear (eighth) cranial nerve. The cell bodies of these bipolar vestibular affer the vestibular gan glion (the Scarpa ganglion), which lies in the internal acoustic meatus (Fig. 4). The ce these bipolar cells enter the brainstem and terminate in the ipsilateral vestibular nuclei and cerebellum.

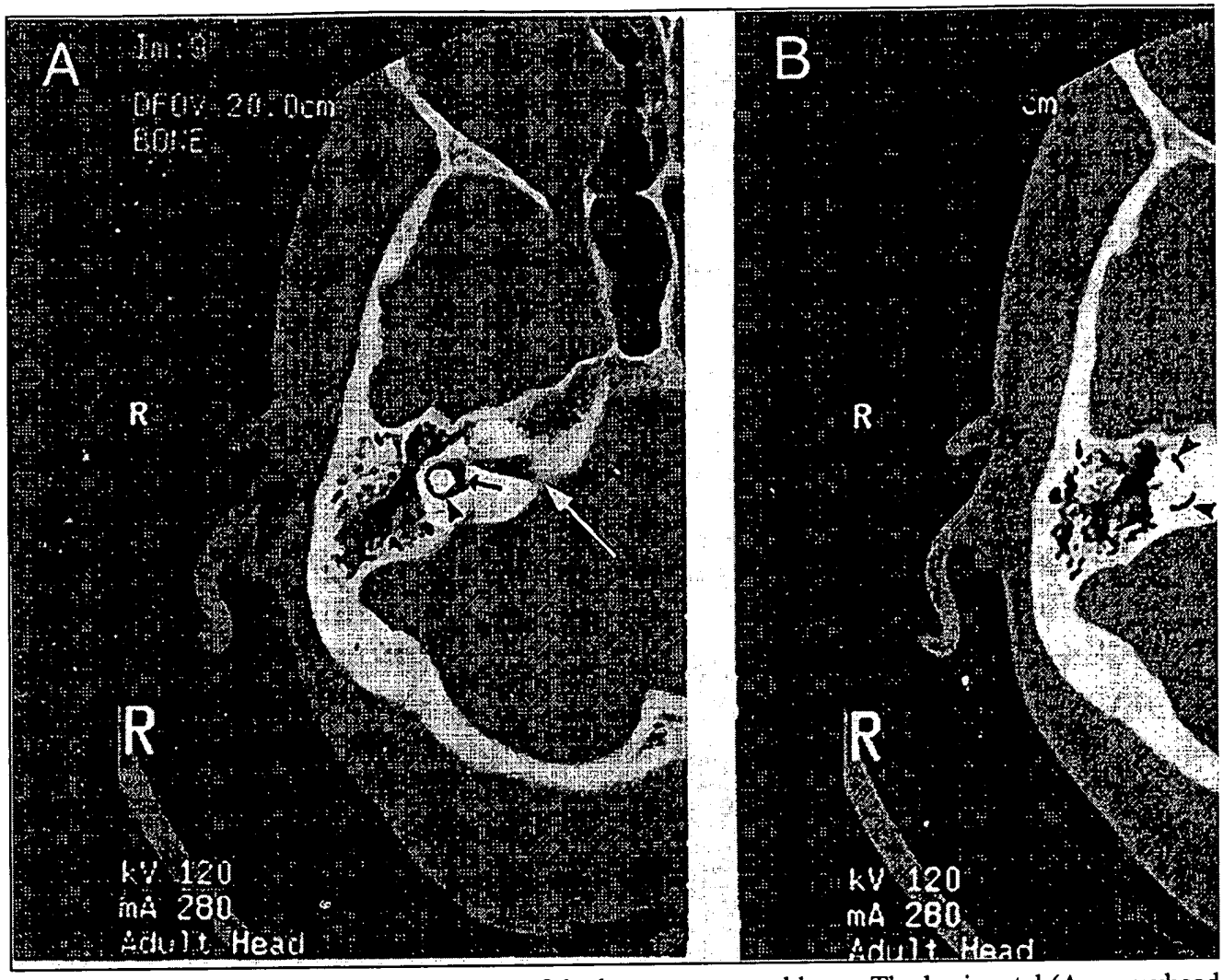

Figure 4. Computed tomography (CT) scans of the human temporal bone. The horizontal (A, arrowhead posterior (B, arrow heads) semicircular canals, utricle (A, small arrow), and internal acoustic canal (A, l visible.

The blood supply to the labyrinth is primarily via the labyrinthine artery, usually a branch of the anterior cerebellar artery. This vessel enters the temporal bone through the internal auditory meatus. Al though n the labyrinthine artery, the stylomastoid artery also provides branches to the labyrinth, mainly to the sem An interrup tion of blood supply to the labyrinth will compromise vestibular (and cochlear) function, res rinth-associated symptoms such as dizziness, nystagmus, and unstable gait.

Membranous Labyrinth. The membranous labyrinth is supported inside the bony labyrinth by conne three ducts of the semicircular canals connect to the utricle, and each duct ends with a single promi nent ampulla (see Fig. 2). Sensory receptors for the semicircular canals reside in a neuroepithelium at the bas The receptors in the utricle are oriented longitudinally along its base, and in the saccule they are oriented the medial wall (see Fig. 2). Endolymph in the laby rinth is drained into the endolymphatic sinus via sm this sinus communicates through the endolymphatic duct with the endolymphatic sac, which is located a mater (see Fig. 2). The saccule is also connected to the cochlea by the ductus reuniens.

The balance between the ionic contents of endo lymph and perilymph is maintained by spccialized secre membranous labyrinth and the endolymphatic sac. In cases of advanced Ménière disease, there is disrupt endolymph volume resulting in endolymphatic hydrops (an abnormal distention of the membranous laby

of Ménière disease include severe vertigo, positional nystagmus, and nausea. Affected persons often suf attacks of auditory and vestibular symptoms, including vomiting, tinnitus (ringing in the ears), and a con make head movements or even stand passively. For patients with frequent debilitating attacks, the first c is often administration of a diuretic (e.g., hydrochlorothiazide) and a salt- restricted diet to reduce the hy persistent Ménière symptom continues, a second treatment option is the implantation of a small tube or s abnormally swollen endolymphatic sac.

Occasionally a condition may develop in which a portion of the temporal bone overlying either the ante posterior semicircular canal thins so much that an opening (dehiscence) is created next to the dura (Fig. patients, the canal dehiscence exposes the normally closed bony labyrinth to the intradural space. Sympt vertigo and oscillopsia in response to loud sounds (the Tulio phenomenon) or in response to maneuvers middle ear or intracranial pressure. The eye move ments evoked by these stimuli (nystagmus) align with dehiscent superior canal. Surgical closure of the defect by bone replacement is often performed.

Figure 5. Computed tomographic image of the temporal bone projected into the plane of the left superio patient with superior canal dehiscence syndrome. The patient developed vertigo, oscillopsia, and eye mc plane of the left superior canal in response to loud noises and pressure in the left ear. A dehiscence is no left superior canal (arrowhead).

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Neuromodulation and Neural Plasticity

Daniel Casasanto

Neuromodulatory synaptic transmission differs from classical chemical synaptic transmission in both mechanism and function. The function of a classical synapse is to convey information rapidly from the presynaptic neuron to its target cell, producing a short-term effect. The neuromodulatory synapse may do the same initially, but its primary function is to transmit information that will have long-lasting effects on the postsynaptic neuron's metabolic activity, and on its response to subsequent input. These effects are fundamental to the development and adaptation of the nervous system, and are believed to be the basis of such higher functions as learning and memory.

Neurotransmitters released from a classical presynaptic neuron bind to specific receptor proteins in the postsynaptic cell membrane, causing ion channels in the membrane to open or close. If the resulting flow of ions depolarizes the membrane relative to its resting potential, the probability that an action potential will be generated increases, and the synapse is considered excitatory. If the ion flow results in a net hyperpolarization of the membrane, the probability that an action potential will be generated decreases, and the synapse is considered inhibitory. Neuromodulatory synapses can be either excitatory or inhibitory. A neurotransmitter released from the presynaptic neuron may cause the postsynaptic membrane to depolarize or to hyperpolarize by the same mechanism used in classical synapses, but the resulting postsynaptic potential will be relatively weak and slow. Whereas a neurotransmitter in a classical synapse may induce postsynaptic effects lasting from ten to one hundred milliseconds, a neuromodulator's postsynaptic effects may persist from several hundred milliseconds to several hours.

Neuromodulation of the postsynaptic neuron depends not so much on the neurotransmitter as on the receptor to which it binds, called a metabotropic receptor. Whereas classical ionotropic receptors affect postsynaptic membrane permeability directly, metabotropic receptors effect changes in the postsynaptic neuron via intracellular molecules called a second messengers. When a neurotransmitter binds to a metabotropic receptor, a protein inside the postsynaptic cell initiates a cascade of biochemical events that influence the neuron's future response to stimuli. Although the neurotransmitter, or "first messenger," becomes inactivated rapidly, the effects of the second messenger may last several days. One way in which the second messenger induces prolonged effects is by initiating the synthesis of new proteins, which remain in the cytoplasm of the postsynaptic neuron, influencing its activity. Certain proteins can affect the genome of a postsynaptic cell, permanently altering the cell's activities.

Neural plasticity is the ability of neural circuits to undergo changes in function or organization due to previous activity. The simplest example of neural plasticity is facilitation: the increase in amplitude of a

postsynaptic potential due to rapid repeated activation. The facilitated neuron returns to its resting potential between activations, and its enhanced postsynaptic response is fleeting. Potentiation, in contrast, is a special type of facilitation in which an increased postsynaptic potential persists after the facilitating stimulus has subsided. A high frequency burst of presynaptic impulses lasting several seconds, called a tetanic stimulus, can cause a posttetanic potentiation, (PTP) lasting several minutes. Extended tetanization engenders long-term potentiation, (LTP) which can result in elevated postsynaptic activity for hours or days. LTP is sustained, in part, by molecules called retrograde messengers. These molecules are synthesized in the postsynaptic cell as a result of presynaptic events. Retrograde messengers diffuse back into the presynaptic cell, where they stimulate neurotransmitter release. Although homosynaptic potentiation is possible, LTP usually results from heterosynaptic potentiation: the convergence of two or more inputs on a neuron which bears the appropriate type of receptor, called an NMDA receptor. Although this receptor is ionotropic, LTP is a neuromodulatory process, in which serotonin commonly serves as the neuromodulator, and cAMP is the second messenger.

Although early neural development is largely gene-dependent, neural plasticity is necessary for the functioning of activity-dependent circuits: systems which only develop if properly stimulated by neuronal activity resulting from an organism's exposure to its environment. Studies conducted on kittens in which one eye was occluded during the developmental critical period suggest that processes associated with binocular vision depend upon a kind of LTP, mediated by NMDA receptors. Extrinsic stimuli that cause activation of the developing pathways must accompany intrinsic developmental mechanisms.

Developmental plasticity is observed commonly in maturing organisms, but is also evident in adults. Experiments involving two groups of rats, one raised in a "simple" environment with few stimuli, the other raised in a "complex" environment with many stimuli, evince activity-dependent development. Predictably, the rats raised in the complex environment demonstrated enhanced neural development relative to those raised in the simple environment. Surprisingly, rats raised in a common environment until adulthood showed developmental differences upon separation into simple and complex environments. Rats placed in a complex environment after the critical period showed enhancements similar to those demonstrated by rats raised in the complex environment: increased cortical mass, increased dendritic branching and complexity, and an increased number of synapses per neuron. Enhancements appeared within a week of the rats' placement in the complex environment. Although not all developmental effects seen in young rats were observed in adults, these experiments show that structural changes occur in the nervous systems of adult organisms when they experience new stimuli.

Learning, a change in an animal's behavior as a consequence of its experience, may be considered at the neuronal level to be an extension of previously described neuromodulatory processes. Habituation, the simplest form of learning, is the decline and eventual cessation of a neuron's response to a repeated stimulus. It is closely related to facilitation. Whereas facilitation is an increase in postsynaptic activity accompanied by increased neuromodulator transmission, habituation is a reduction in postsynaptic response accompanied by reduced neurotransmitter release from the presynaptic neuron. Also related are dishabituation, the recovery of a habituated neuron's responsiveness upon the introduction of a novel strong stimulus, and sensitization, the strengthening of a neuronal response due to some strong stimulus other than the stimulus that usually activates a given neuron. A somewhat more sophisticated type of sensitization is associative conditioning, most memorably demonstrated by Pavlov's dog. The conditioned animal forms an association between two different stimuli which are repeatedly presented in rapid succession. Eventually, the animal begins to exhibit behavior appropriately elicited by one stimulus, even when presented with the other stimulus alone.

A progression from facilitation to these incrementally more complicated processes should be evident. It is not surprising, therefore, that they have a common neuromodulatory mechanism. In invertebrates,

sensory neurons connect with motor neurons via facilitating interneurons. Serotonin is released from the interneurons, triggering the cAMP second messenger to initiate biochemical events whose outcome is observable as a "learned" response. If results of neural plastic adaptations persist, becoming long-lasting changes in neuronal structure or activity, they can be described as memory. There are significantly different types of memory, but all types can be seen as the prolongation of alterations in the nervous system brought about by neuromodulatory processes such as habituation and sensitization. One way in which transient neuromodulation can become memory is through the regulation of protein synthesis in the postsynaptic cell. A neurotransmitter activates a cAMP second messenger, which leads to the binding of a regulatory protein to a DNA strand, which controls the transcription of a gene responsible for protein synthesis. A new protein may help to perpetuate the cells activity, or may induce structural changes such as those giving rise to new synapses. Although these processes involved in memory formation are well understood, many questions remain regarding the storage and retreival of what organisms learn. Perhaps what is known about the neuromodulatory events underlying learning and memory will help neuroscientists to continue learning about their mysteries.

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